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10/532,580	04/25/2005	Jin-Hoi Kim	P27726	4797

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EXAMINER	
MAKAR, KIMBERLY A	
ART UNIT	**PAPER NUMBER**
1636	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/532,580	KIM, JIN-HOI	
	Examiner	Art Unit	
	Kimberly A. Makar, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-61* is/are pending in the application.

4a) Of the above claim(s) *26-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 April 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/12/05; 12/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. Applicant's election with traverse of group I in the reply filed on 2/28/07 is acknowledged. The traversal is on the ground(s) that the restriction is improper because (1) all claims are dependent upon the claims of group I, and the PCT Rules state that dependent claims cannot be considered for unity of invention purposes; (2) the Examiner used the improper critierion of distinctness for groupings under 371 practice; and (3) all claims chare a common technical feature and all claims ultimately depend from one independent claim. This is not found persuasive because:

2. Claims drawn to different and distinct categories were properly restricted between "dependent" claims. The MPEP Chapter 800 states:

3. Unity of invention has to be considered in the first place only in relation to the independent claims in an international application and not the dependent claims. By "dependent" claim is meant a claim which contains all the features of one or more other claims and contains a reference, preferably at the beginning, to the other claim or claims and then states the additional features claimed (PCT Rule 6.4). The examiner should bear in mind that a claim may also contain a reference to another claim even if it is not a dependent claim as defined in PCT Rule 6.4. One example of this is a claim referring to a claim of a different category (for example, "Apparatus for carrying out the process of Claim 1 ...," or "Process for the manufacture of the product of Claim 1 ..."). Similarly, a claim to one part referring to another cooperating part, for example, "plug for cooperation with the socket of Claim 1 ...") is not a dependent claim.

4. Thus while claims 26-61 were "dependent" in that they referenced another claim, they were claims in different categories. Thus, even though they share a common technical feature, they are not true dependent claims as defined in PCT rule 6.4. Additionally, the claims 26-61 were not grouped separately simply because they were in a different category, but the restriction provided support for the groupings showing how

the different categories could be used in alternative methodologies and compositions. Thus the "distinctness" was used merely to draw the attention of Applicant to the different categories of the "dependent" claims.

The requirement is still deemed proper and is therefore made FINAL.

5. Claims 26-61 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/28/07.

Specification

6. The disclosure is objected to because of the following informalities: The specification lists 2 example 6's but is missing an example 5 (page 29 and 30).

Appropriate correction is required.

Drawings

7. The drawings are objected to because Figures 8-10 are unclear. Figures 8-9 have vectors names listed as I/pUPII/hEPO (IUP2), pUPII/hEPO/WPRE (PW) and I/pUPII/hEPO/WPRE (IW) respectively. However the figure legend in the specification all recite that these figures "show the structure of vector pUP2/hEPO." Thus the figure lengend does not correlate with the figures. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or corrected figure legends that reflect the drawings are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate

prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

8. Claim 24 is objected to because of the following informalities: claim 24 is grammatically incorrect. Claim 24 is missing a period at the end of the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 13-14 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 13-14 recite "a porcine II gene promoter" and mutations of that promoter and read on a product of nature. SEQ ID NO:1 is a natural sequence found in nature isolated from the porcine genome. The scope of the claim, therefor, encompasses a product of nature, which is non-statutory subject matter. As such, the recitation of the limitation "recombinant" or "isolated" would be remedial. See 1077 O.G. 24, April 21, 1987.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 14, 16, 18, 21, 23, are 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

13. The claims read on a uroplakin II promoter selected from functional equivalents which have one or more disruption, deletion, insertion, point substitution, nonsense, missense, polymorphism or rearrangement mutations occurred in the base sequence of

SEQ ID NO:1, and expression vectors comprising that promoter. The claims therefor read on a genus of promoters and expression vectors.

14. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

15. The instant claims, construed as discussed herein above, embrace a promoter and expression vector comprising an isolated porcine Uroplakin II promoter according to SEQ ID NO. 1, which have one or more changes, including disruption, deletion, insertion, point, substitution, nonsense, missense, polymorphism or rearrangement mutation, wherein the structural characteristics of the claimed regulatory promoter are essentially unlimited.

16. The Guidelines for Written Description state "The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art" (*Federal Register*/ Vol. 66, No. 4/Friday, January 5, 2001/Notices, column 1, page 1105). The Guidelines further state, "[t]he claim as a whole, including all limitations found in the preamble, the transitional phrase, and the body of the claim, must be sufficiently supported to satisfy the written description requirement" (at page 1105, center column, third full paragraph). An applicant shows possession of the claimed

invention by describing the claimed invention with all of its limitations. *Lockwood v. American Airlines Inc.* (CA FC) 41 USPQ2d 1961 (at 1966).

17. The Guidelines further state: "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus" (*Federal Register*, Vol. 66, No. 4, Column 3, page 1106). "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus" (MPEP §2163(3)(a)(ii)).

18. The Guidelines further state, "[s]atisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the genus in view of the species disclosed" (Id. at 1106, column 3).

19. In the instant case, the application discloses a porcine Uroplakin II promoter and expression vector comprising that promoter. In the instant case, applicants have provided 6 working examples of vectors all comprising the full length porcine Uroplakin II promoter having the nucleotide sequence of SEQ ID NO: 1. Applicants do not disclose any working examples of porcine Uroplakin II promoters which are functional equivalents of SEQ ID NO 1. Applicants do not test fragments of the porcine uroplakin

promoter, perform mutagenesis on the promoter, nor disclose structural or functional regions within the Uroplakin II promoter.

20. Are there minimal regions of the promoter required for expression? Which ones? Would the insertion of any nucleotide disrupt the function of such a region? The promoter of SEQ ID NO. 1 is over 8 kb in length. Applicants have not provided any clues to specific characteristics of the promoter nucleotide region with a functional motif. There are hundreds to thousands of potential promoters possible from functional equivalents which have one or more disruption, deletion, insertion, point substitution, nonsense, missense, polymorphism or rearrangement mutations occurred in the base sequence of SEQ ID NO:1. Therefore, it is not clear that the sequences set forth in the sequence listing are actually species of the invention.

21. Even if one is to assume, *arguendo*, that the functional properties recited in the instant claims are inherent to the nucleic acids set forth as SEQ ID NO:1, these species are not representative of the broad genus claimed because they clearly do not convey the necessary common attributes or features of essentially any nucleic acid having the recited function.

22. Furthermore, with regard to the "relevant identifying characteristics" of the claimed invention, the specification provides no disclosure of the structural features that define the function recited in the claims. As stated in MPEP 2163(I)(A), a biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes. Thus, applications

that seek to claim biological molecules having a defined function and broadly divergent structure must disclose a correlation between that function and a corresponding structure.

23. There is no evidence presented by application that the any alteration to the sequences of SEQ ID NO: 1 are sufficient to define a genus of any nucleic acid capable of promoter activity as presently claimed. Therefore, the application also fails to provide the relevant identifying characteristics of the claimed invention.

24. An adequate written description of a method and composition utilizing DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself. It is not sufficient to define DNA solely by its principal biological property (i.e., it is capable of promoter activity) because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming a methodology or composition in which all DNA's that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

25. In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession

of the claimed invention because it does not provide adequate written description for the broad class of any functional equivalents which have one or more disruption, deletion, insertion, point substitution, nonsense, missense, polymorphism or rearrangement mutations occurred in the base sequence of SEQ ID NO:1. Therefore, the claims are properly rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description.

26. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

27. Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 19 requires the use of the vector pUP2/hEPO deposited under accession number KCTC 10352BP. The specification nor the claims do not teach the skilled artisan how to reliably reproduce the same vector. While the claim recites the Korean Collection for Type Cultures (KCTC), Korean Research Institute of Bioscience and Biotechnology accession numbers, a statement by applicants, the assignee or applicants' representative indicating that all restrictions on the availability of the deposited materials

will be irrevocably removed upon the granting of a patent on the instant application is required.

28. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

29. Claims 20-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

30. Claims 22-25 recite the phrase "a WPRE of SEQ ID NO:7." It is unclear "a WPRE of SEQ ID NO:7" is a separate nucleotide sequence which is responsive to SEQ ID NO:7, or if SEQ ID NO:7 is the WPRE sequence? Thus does it refer to "the WPRE of SEQ ID NO:7" or "a WPRE as represented by SEQ ID NO:7" or "a WPRE consisting of SEQ ID NO:7"? A skilled artisan would be unable to determine the metes and bounds of the claimed invention.

31. Claims 20-21, 24-25 recite the phrase, "an insulator of SEQ ID NO: 6." It is unclear if this refers to an insulator of SEQ ID NO:6, as in a separate nucleotide sequence which insulates SEQ ID NO:6, or if SEQ ID NO:6 is the insulator sequence? Thus does it refer to "the insulator of SEQ ID NO:6" or "an insulator as represented by SEQ ID NO:6" or "an insulator consisting of SEQ ID NO:6"? A skilled artisan would be unable to determine the metes and bounds of the claimed invention.

32. It is noted that this Office Action contains rejections of the same claims under 35 USC 112, 1st (written description) and 35 USC 102 (a). While these rejections may

seem contradictory, they are not because each is based upon a different legal analysis, i.e. sufficiency of the disclosure of the instant application to support claims under 35 USC 112, 1st paragraph vs. sufficiency of a prior art disclosure to anticipate or render obvious an embodiment(s) of the claimed invention (See *In re Hafner*, 161 USPQ 783 (CCPA 1969)).

Claim Rejections - 35 USC § 102

33. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

34. Claims 13-14 are rejected under 35 U.S.C. 102(a) as being taught by Kwon et al (Cloning, sequencing and expression analysis of the porcine uroplakin II gene. Biochemical and Biophysical Research Communications, 2002. 293:862-869) (of record 1/30/07). Claims 13-14 recite a porcine uroplakin II gene promoter having a base sequence of SEQ ID NO:1 (claim 1) and the uroplakin I promoter of claim 13, which is one selected from functional equivalents which have one or more disruption, deletion, insertion, point, substitution, nonsense, missense, polymorphism or rearrangement mutation occurred in the base sequence of SEQ ID NO:1. These claims are not limited to "the" base sequence of SEQ ID NO:1, but are interpreted as a promoter having "a" base sequence of SEQ ID NO:1. This reads on *any* nucleotide found within SEQ ID NO:1 that is a porcine uroplakin II gene promoter.

35. Kwon et al teaches the cloning and sequencing of the 9 kb genomic region of the porcine 5' UTR of uroplakin II regions (page 864, column II, last paragraph). Kwon also discloses a portion of that sequence in figure 2, submitted to Genbank as accession no. AY044180). Thus Kwon teaches the claimed invention.

Claim Rejections - 35 USC § 103

36. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

37. Claims 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kwon et al (Cloning, sequencing and expression analysis of the porcine uroplakin II gene. Biochemical and Biophysical Research Communications, 2002. 293:862-869) as applied to claims 13-14 above, further in view of Sun (US Patent 6,339,183) listed in applicants IDS dated 9/12/05. Claims 15-18 recite an expression vector comprising a porcine uroplakin II promoter having a base sequence of SEQ ID NO:1 or one selected from functional equivalents and a base sequence encoding a target protein at the 3' end of the promoter, wherein the target protein is human erythropoietin.

38. Kwon et al teaches a porcine uroplakin II promoter comprising a base sequence of SEQ ID NO: 1 (see above). Kwon teaches the uroplakin II promoter could be used to transform the bladder, which in turn "could provide an alternative to the mammary gland

for heterologous protein production" (page 868, column I, first paragraph, last sentence). Kwon does not teach that the promoter is used to drive the heterologous expression of human erythropoietin.

39. Sun (US Patent 6,339,183) teaches a vector which contains a promoter construct linked to a heterologous gene encoding a selected biological active molecule wherein the promoter is capable of directing urothelial expression of the heterologous gene (see abstract). Sun teaches that the promoter is the Uroplakin II gene promoter from mouse (column 4-6) but teaches that the uroplakin II promoter from other animals can also be used, and includes other animals of uroplakin II gene expression includes pigs (column 4, lines 2-9 and column 7, lines 1-8) stating, "[t]here is sufficient similarity between this gene in different species, so that similar results with the UPII promoter sequence in other animals is expected" (column 7, lines 5-8). Sun teaches that the lacZ gene is ligated downstream (at the 3' end) of the uroplakin II promoter (see figure 3B), but that other heterologous genes can be substituted for LacZ, including Erythropoietin.

40. A skilled artisan would have been motivated to combine the teaching of Kwon on a porcine II promoter that can be used to drive heterologous protein expression from the bladder further with the teaching of Sun on an expression vector wherein the therapeutic gene erythropoietin is driven by a porcine uroplakin II protein because while Sun does not disclose the specific sequence of the pig's uroplakin II promoter, he teaches that the similarity between species would result in similar heterologous expression results. It would have been obvious to the skilled artisan to combine the teaching of Kwon on a porcine II promoter with the teaching of Sun on an expression

vector wherein the therapeutic gene erythropoietin is driven by a porcine uroplakin II promoter for the expected benefit of utilizing alternate species promoters for additional ways to express therapeutic genes with similar success as taught by Sun. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the instant invention was made, it must be considered that said ordinary skilled artisan would have had reasonable expectation of success in practicing the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Makar, Ph.D. whose telephone number is 571-272-4139. The examiner can normally be reached on 8AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D. can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kam/5/10/07

DAVID GUZO
PRIMARY EXAMINER